REMARKS

Claims 1, 2, 4-9, 12, 14, 15, 28, 30-36, 43 and 47-56 are pending in the application. Claims 10 and 11 have been cancelled. Claims 1, 2, 4-9, 12, 14, 28, 36, 43 and 47-54 are currently amended. Claims 55 and 56 are new claims.

The specification is amended in response to Examiner's objection to the inconsistent statements in the previous version of specification. The specification is also amended to clarify the definitions of some terms used in the application. No new matter is present in the specification as amended.

I. Specification Objections

Applicant is submitting a clean substitute specification (Appendix A) and a mark-up copy (Appendix B) along with this response because Examiner indicates that no amended Specification has been received along with Applicant's last response. All objections raised by Examiner in the last two Office Actions are addressed in this response. The specification is objected to for multiple reasons. Applicants have amended the specification to overcome these objections as explained in the following text.

(A) The specification is objected to because the disclosure for the structure of the AviIII polypeptide is unclear. Applicant has amended the specification so that the delineation of the domain structure is consistent with the structure represented in Figure 1 as originally filed.

(i) The specification on page 5, paragraph 5 has been amended by deleting reference to CBD_II and FN_III domains.

(ii) The specification on page 16, paragraph 4 to page 17, paragraph 1 has been amended so that the numbering of amino acids is consistent with SEQ ID NO. 1.

(iii) The inconsistency is resolved by the amendment in (ii) above.

(iv) The inconsistency is resolved by the amendment in (ii) above.

(B) Examiner has objected to the specification because the phrase "substrate targeting moiety" is unclear. The specification on page 14 has been amended to clarify that "Substrate targeting moiety" refers to any signal on a substrate, or any signal on other molecules (or ligand) bound to such a substrate, used to target any AvilII polypeptide or fragment thereof to a substrate. Applicants believe that the amendment should render the definition of "Substrate targeting moiety" clear and unambiguous.

(C) All hyperlinks have been deleted in the Specification.

II. Claim Objections

Claims 47, 50, 53 and 54 have been amended according to the Examiner's suggestion. Withdrawal of the objections is respectfully requested.

III. Claim Rejections—35 U.S.C. 112 second paragraph

Claims 1, 2, 4-11, 14, 15 and 47-54 are rejected under 35 U.S.C. §112 second paragraph as being indefinite. The Examiner states that the phrase "AvilII peptide" renders the claims indefinite. Claims 10 and 11 have been cancelled, Claims 1, 2, 4-9, 14, 15 and 47-54 have been amended and the

phrase "AviIII peptide" has been replaced with the word "polypeptide" to overcome this rejection.

Examiner also rejected Claims 1, 2, 4-11, 14, 15 and 47-54 because the phrases "a catalytic domain of a glycosyl hydrolase family 74 (GH74_Ace) enzyme" and "carbohydrate binding domain (CBD)III" render the claims indefinite. With regard to claim 1, these features of the claim have now been moved to claim 2, and the dependant claims have been amended to reflect this change. Claims 10 and 11 have been cancelled. Claims 47-54 retain use of these terms.

The Examiner states that the specification fails to define the structure of both the GH74 and the CBD III domains; however, this is untrue. It is indisputable that the art well recognizes the features of GH74 and CBD III type family domains. The Court of Appeals For The Federal Circuit has recently issued an opinion stating that, as to the *Lilly*- style written description or enablement issues, the Applicant need not specifically teach what is well known and recognizing that it is acceptable to claim a large number of non-specifically disclosed sequences that may be produced by techniques which are well known and advanced in the art:

> The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization.

Capon v. Eshar, 76 USPQ2d 1078, 418 F3d 1349 (Fed. Cir 2005).

Furthermore, Applicant has described species of these family domains that are particularly claimed. These are inherent to the sequence that is claimed, for example, as set forth in Table 4 on page 6 of the specification as filed. The specification (as amended) clearly points out the structure of the GH74 domain as shown both in SEQ ID NO. 1 and SEQ ID NO. 3. Similarly, the structure of the CBD III domain is well defined by the text of the specification, Table 2 and Fig. 1. Withdrawal of the rejection of Claims 1, 2, 4-9, 14, 15 and 47-54 based on 35 U.S.C. §112 second paragraph is respectfully requested.

Examiner further rejects Claim 31 under 35 U.S.C. §112 second paragraph for reciting "substrate targeting moiety." The Examiner also states that the term "substrate" is not defined in the specification. Applicant respectfully traverses this assertion. On page 9, last paragraph of the currently amended specification, "substrate" is defined as "a polymer such as cellulose or can be a complex molecule or aggregate of molecules where the entire moiety comprises at least some cellulose." A cellulase naturally targets a cellulose substrate. Withdrawal of the rejection of Claim 31 based on 35 U.S.C. §112 second paragraph is respectfully requested.

Claims 1, 2, 4-12 and 47-54 are rejected under 35 U.S.C. §112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention because the phrase "substantially purified" renders the claim indefinite. Claims 10 and 11 have been cancelled. The other claims have been amended and the word "substantially"

has been deleted for purpose of clarification. Withdrawal of the rejection of these claims based on 35 U.S.C. §112 second paragraph is respectfully requested.

Claim 6 is rejected under 35 U.S.C. §112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 has now been amended to clarify the subject matter which Applicant intends to claim. Withdrawal of the rejection of Claim 6 based on 35 U.S.C. §112 second paragraph is respectfully requested.

Claim 12 is rejected under 35 U.S.C. §112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 has been amended and withdrawal of the rejection based on 35 U.S.C. §112 second paragraph is respectfully requested.

IV. Claim Rejections—35 U.S.C. §112 first paragraph-Enablement

Claims 1, 2, 4-11, 14, 15, 28, 30-36, 43 and 53 are rejected under 35 U.S.C. §112 first paragraph for lack of enablement. Examiner states that these claims are so broad as to encompass any polypeptide having at least 90% identity with SEQ ID NO: 1 or SEQ ID NO: 3. Applicant respectfully disagrees with the Examiner for the same reasons set forth in previous responses.

"It is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention." *Capon, Id.* Applicant notes that claims which now recite a 99% sequence identity to SEQ ID NO: 1 are not rejected by Examiner for lack of enablement (*See, e.g.*, Claim 49). Applicant has modified the percent identity from 90% to 99% in Claim

1 and 53. Claim 28 has also been amended so that it now recites a polypeptide containing a sequence identical to either of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5. Claims 10 and 11 have been cancelled. Claims 2, 4-9, 14, 15, 30-36 and 43 all depend from Claim 1 or Claim 28 either directly or indirectly. Applicant believes these amendments should overcome Examiner's rejection for lack of enablement. Withdrawal of the rejection based on 35 U.S.C. §112 first paragraph is respectfully requested.

V. Claim Rejections—35 U.S.C. §112 first paragraph--written description

(1) Claims 10 and 11 are rejected under 35 U.S.C. §112 first paragraph for insufficient written description. Claims 10 and 11 have been cancelled.

(2) Claims 28, 30-36 and 43 are rejected under 35 U.S.C. §112 first paragraph for insufficient written description. Claims 28 has been amended to be directed to polypeptides having at least 99% identity to either of SEQ ID NO: 1, NO: 3, NO: 4 or NO: 5. Withdrawal of rejections for insufficient written description under 35 U.S.C. §112 first paragraph is respectfully requested.

VI. Claim Rejections—35 U.S.C. §102

Claims 1, 2, 4-12, 14, 15, 28, 36, 43 and 47-54 stand rejected under 35 U.S.C. §102(b) as being anticipated by Adney et al., 1994 or Tucker et al. 1989. Examiner stated that both of Adney and Tucker teach a composition comprising the culture supernatant of *Acidothermus cellulolyticus*. Examiner's reasons that

the culture supernatant more likely than not contains the cellulase of SEQ ID NO: 1 because (a) the cellulase is made by *A. cellulolyticus*; and (b) the cellulase has a signal sequence and would be secreted from the cell. Examiner, however, has not provided any evidence showing why a person of ordinary skill would believe that both (a) and (b) are likely to be true before the present disclosure was made.

First, there is no evidence that at the time before the present invention, it was known that the genome of *A. cellulolyticus* contains a gene encoding the polypeptide of SEQ ID NO: 1. Even if the AviIII gene were known to exist, it had not been shown that the polypeptide of SEQ ID NO: 1 is expressed under the condition of Adney or Tucker. Therefore, even assuming that what the Examiner argues may be true, there is no showing that this unrecognized peptide was ever purified as is claimed. The rejection is too speculative to withstand scrutiny and cannot be maintained. Applicant does not understand why the Examiner insists that a person of ordinary skill would believe that the culture supernatant in Adney or Tucker more likely than not contains the claimed purified polypeptide of SEQ ID NO: 1.

Secondly, it was not until the present invention was made when it became known that the polypeptide of SEQ ID NO: 1 contains a signal peptide which facilitates secretion of the enzyme into the culture media. Applicant again fails to understand why Examiner insists that a person of ordinary skill would believe that the polypeptide of SEQ ID NO: 1 has a signal sequence and would be secreted from the cell. According to Examiner's rationale, if someone in the past has collected all human blood cells and homogenize them into a mixture of

thousands of molecules, no patents would be issued to inventors who later identify novel purified sequences of hormones, cytokines, and cell surface receptors expressed by human blood cells, because all these novel molecules more likely than not exist in the cell homogenate.

Even if we assume that a person of ordinary skill would believe that the cellulase is made by *A. cellulolyticus*; and that the cellulase has a signal sequence and would be secreted from the cell, the present claims are not anticipated by Adney or Tucker because neither reference teaches all the limitation of the amended claims.

The culture supernatant of Adney or Tucker was a crude mixture of many proteins and Examiner has provided no evidence that the culture supernatant had been purified within the meaning of the present invention. Therefore, neither Adney nor Tucker teaches all the limitations of the present claims and withdrawal of the rejection under 35 U.S.C. 102(b) is respectfully requested.

VII. Claim Rejections—35 U.S.C. §103

Claims 1, 2, 4-12, 14, 15, 28 and 47-54 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Mohaghegi et al. 1986 in view of Berghem et al. 1976 and Katz et al. 1968. Mohaghegi et al. 1986 is said to show the isolation of *Acidothermus cellulolyticus*, but not the isolation of cellulase therefrom. Berghem et al. 1976 is used to show the isolation of an endoglucanase from *Trichoderma viride*. Katz et al. supposedly shows motivation to combine, since it is desirable to generate alternative cellulases capable of commercial scale

processing at elevated temperatures. We respectfully traverse because the Office has not shown a *prima facie* case of obviousness.

"To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *See* MPEP 2143.03. At present, no reference teaches or suggests the GH74 family polypeptide that is claimed. This is an *exoglucanase* or modified exoglucanase, for example, as shown in SEQ ID NO. 1. In contrast, Mohaghegi et al. 1986 in view of Berghem et al. 1976 and Katz et al. 1968 uses Berghem et al. to show the isolation of a cellulase, but the cellulase is an *endoglucanase*. Therefore, this cannot be the GH74 family polypeptide that is claimed. As Paragraph 9 of the Rule 132 Declaration filed December 26, 2002 makes clear, the claimed GH74 domain functions as an exoglucanase, not an endoglucanase. It follows that the combination does not teach or suggest all of the claim limitations because the combination, if proper, would merely result in the isolation of an endoglucanase from *A. celllulolyticus*. Therefore, Mohaghegi et al. 1986 in view of Berghem et al. 1976 and Katz et al. 1968 does not teach or suggest the isolation of an exoglucanase of SEQ ID NO: 1 as presently claimed.

Furthermore, in order to establish a *prima facie* case of obviousness, the references must provide sufficient guidance and enabling methodology for practicing the claimed invention with reasonable expectation of success. Applicant presented reasoning in the last response that Mohaghegi et al., Berghem et al. and Katz et al., taken together, do not teach or suggest purification of the enzyme to the extent disclosed by the instant application.

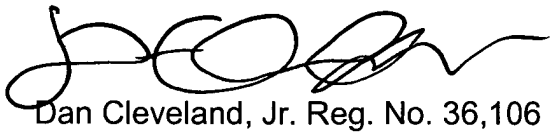
By disclosing the coding sequence of AviIII, the present invention enables one to overexpress AviIII in a heterologous host through genetic engineering. Thus it is now possible to maneuver the host cells so that the amount of AviIII is much greater than any co-purifying protein in the starting materials. Even if these co-purifying proteins are still difficult to remove through conventional biochemical methods, a "purified" preparation containing more than 90% of AviIII can be achieved because the starting materials contain a much greater amount of the target protein by overexpression. There is no indication that Mohaghegi et al., Berghem et al. and Katz et al., taken together have achieved this level of purity. The rejection is speculative, especially as regards co-purification, and the references do not stand for the propositions to which the Examiner has applied them.

Without a showing of purity commensurate with that of the present invention, the three references, taken as a whole, do not provide enabling methodology with reasonable expectation of success to motivate one of ordinary skill to attempt to prepare the exoglucanase of the present invention to a purity of about 90%. Applicants respectfully request withdrawal of the 35 U.S.C. §103 rejections.

Applicant's representative believes that the amendments presented in this response place all pending claims in condition for allowance. The Commissioner is authorized to charge any additionally required fees to deposit account 14-0460. Should the Examiner have any questions, comments, or suggestions that would expedite the prosecution of the present case to allowance, Applicant's

representative, Paul White, earnestly requests a telephone call at (303) 384-7575.

Respectfully submitted



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